Amendments to the Claims:

This listing of claims will replace all prior versions, and listings, of claims in the application:

1. (Currently Amended) A process for determining whether a test compound specifically binds to and modulates one or more cell~~ular~~ surface receptor proteins, comprising the steps of:

(a) contacting test cells, co-expressing ~~(i)~~ a cell surface receptor protein and ~~(ii)~~ a neurotransmitter transport protein specific for a ligand of said cell surface receptor protein, wherein said test cells produces a second messenger response upon activation of the surface protein, with (i) ~~the~~ a test compound, (ii) ~~and~~ a second compound known to activate the metabotropic glutamate receptor under conditions suitable for activation of the cell surface receptor protein, and (iii) ~~a~~ control cells ~~population~~, wherein said control cells do not express a functional cell surface receptor protein[[,]];

(b) measuring the second messenger response in the control cells ~~population~~ to obtain a first value and in the test cells ~~population~~ to obtain a second value[[,]]; and

(c) comparing the values obtained in (b), wherein if the second value is greater than the first value it indicates that the test compound activates the ~~target~~ cell surface receptor protein, and wherein if the first value is greater than the second value it indicat~~inges~~ that the test compound inhibits activation of the ~~target~~ cell surface receptor protein.

2. (Currently Amended) The process according to claim 1, wherein said ~~target~~ cell surface receptor protein is a human metabotropic glutamate receptor selected from the group consisting of mGluR-1, -2, -3, -4, -5.,-6,-7 and -8.

3. (Currently Amended) The process of claim 1, wherein the second messenger response comprises a change in intracellular calcium levels, wherein said ~~and the~~ change in second messenger response is an increase in the measure of intracellular calcium in the test cells ~~population~~ relative to the control cells ~~population~~.

4. (Currently Amended) The process of claim 1, wherein the second messenger response comprises the release of inositol phosphate, wherein said ~~and the~~ change in second messenger response is an increase in the level of inositol phosphate in the test cells ~~population~~ relative to the control cells ~~population~~.

5. (Currently Amended) The process of claim 1, wherein the second messenger response comprises the release of cyclic AMP (cAMP), wherein said ~~and the~~ change in second messenger

response is a ~~decerase~~ decrease in the level of cAMP in the test cells ~~population~~ relative to the control cells ~~population~~.

6. (Canceled)

7. (Original) The process according to claim 1, wherein said metabotropic glutamate receptor is a human metabotropic glutamate receptor.

8. (Currently Amended) A mammalian cell-based assay for the profiling and screening of putative modulators of one or more human metabotropic glutamate receptor proteins, comprising:

(a) contacting a cell population comprising a plurality of cells co-expressing at least one functional human metabotropic glutamate receptor subtype or a variant, fragment or functional equivalent thereof, and a functional non-human neurotransmitter transport protein or a variant, fragment or functional equivalent thereof specific for a ligand of said receptor and preloaded with a membrane potential fluorescent dye, with (i) at least one modulating moiety whose ability to modulate the activity of the receptor protein is sought to be determined and (ii) a known agonist of said receptor protein; and

(b) monitoring changes in the fluorescence of the cells in the presence of the modulating moiety compared to changes in the absence of the modulating moiety to determine the extent of human metabotropic glutamate receptor modulation.

9. (Original) The assay method of claim 8 in which the test cell is selected from the group consisting of MOCK, HEK293, HEK293T, BHK, COS, NIH3T3, Swiss3T3 and CHO.

10. (Original) The assay method of claim 8 in which the known agonist is added prior to, concurrently or after addition of the modulating moiety.

11. -18. (Canceled)

19. (Original) The assay of claim 8 wherein said fluorescent dye is a calcium-sensitive fluorescent dye.

20. (Canceled)

21. (Currently Amended) The assay of claim 8 wherein said ~~instrument is~~ changes in the fluorescence is measured by use of a ~~fluorescence~~ fluorometric imaging plate reader (FLIPR) or a voltage ion probe reader (VIPR).

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22. (Canceled)

23. (Currently Amended) A method for identifying a modulator of one or more mammalian metabotropic glutamate receptor proteins, comprising:

(a) providing a cell population ~~containing~~ comprising a plurality of recombinant test cells modified to contain the DNA of (i) ~~a~~ at least one mammalian glutamate receptor subtype, or a variant, fragment or functional equivalent thereof, which is operably linked to control sequences for expression, and whose activation can be coupled to a Ca^{2+} signaling pathway, and (ii) a functional non-human neurotransmitter protein or a variant, fragment or functional equivalent thereof, specific for a ligand of said receptor;

(b) providing at least one compound or modulating moiety whose ability to modulate the activity of a metabotropic glutamate receptor protein is sought to be determined[[,]];

(c) incubating or contacting ~~the~~ said cell population with the compound or modulating moiety and a calcium sensitive-fluorescent dye to form a first mixture;

(d) measuring the fluorescence from the calcium-sensitive fluorescent dye in the first mixture in a fluorometric imaging plate reader (FLIPR) to obtain a first value;

(e) repeating steps (a)-(c) ~~except~~ to obtain a second mixture, except that the cell population of step (a) comprises cells that do not express a functional metabotropic glutamate receptor protein;

(f) measuring the fluorescence from the calcium-sensitive fluorescent dye in the second mixture in a fluorometric imaging plate reader (FLIPR) to obtain a second value; and

(g) comparing the fluorescence measurement from (d) with the fluorescence measurement of (f), wherein if the first value ~~in the first mixture~~ is greater than that of the second ~~mixture~~ value, then said ~~at least one test~~ compound or modulating moiety is a positive modulator of the metabotropic glutamate receptor protein.

24. (Currently Amended) A method for identifying a metabotropic glutamate negative allosteric modulator of one or more metabotropic glutamate receptor subtypes having inhibitory activity, said method comprising ~~the steps of~~:

(a) exposing a cell population comprising a plurality of cells co-expressing at least one functional metabotropic glutamate receptor subtype, or a variant, fragment or functional equivalent thereof, and a functional non-human neurotransmitter transport protein, or a variant, fragment or functional equivalent thereof, to ~~the~~ a candidate agent in the presence of a known metabotropic glutamate agonist, wherein said cells produces a second messenger response upon activation of the metabotropic glutamate receptor subtype, under conditions and for a time sufficient to allow interaction of the agonist with the receptor and an associated activation of the metabotropic glutamate receptor, and

(b) detecting an inhibition of the second messenger response by the agonist resulting from the interaction of the candidate agent with the metabotropic glutamate receptor subtype, relative to the second messenger response induced by the glutamate agonist alone, and therefrom determining the presence of a glutamate allosteric modulator having antagonist-like activity.

25. (Currently Amended) The process of claim 24, wherein said ~~test~~ cell population constitutively expresses the mGluR5 receptor subtype.

26. (Original) The method according to claim 24, wherein said metabotropic glutamate receptor subtype is mGluR4.

27. (Currently Amended) A method for identifying a metabotropic glutamate positive allosteric modulator of one or more metabotropic glutamate receptor subtypes having antagonistic activity, said method comprising ~~the steps of~~:

(a) exposing a cell population comprising a plurality of cells co-expressing at least one functional metabotropic glutamate receptor subtype, or a variant, fragment or functional equivalent thereof, and a functional non-human neurotransmitter transport protein, or a variant, fragment or functional equivalent thereof, to ~~the~~ a candidate agent in the presence of a known metabotropic glutamate agonist, wherein said cells produces a second messenger response upon activation of the metabotropic glutamate receptor subtype, under conditions and for a time sufficient to allow interaction of the agonist with the receptor and an associated activation of the metabotropic glutamate receptor, and

(b) detecting activation of the second messenger response by the agonist resulting from the interaction of the candidate agent with the metabotropic glutamate receptor subtype, relative to the second messenger response induced by the glutamate agonist alone, and therefrom determining the presence of a metabotropic glutamate allosteric modulator having agonist-like or activating activity.

28. (Currently Amended) A process for screening a candidate agent for the ability ~~of the candidate agent~~ to positively modulate one or more metabotropic glutamate receptor subtype mediated signal transmission pathway in a mammalian cell comprising:

(a) ~~incubating~~ transforming a test cell population ~~with a candidate agent whose ability to modulate the second messenger activity of the receptor is sought to be determined, wherein said test cell: population is characterized as~~ comprising a plurality of cells co-expressesing a functional metabotropic glutamate receptor subtype glutamate receptor subtype, or a variant, fragment or functional equivalent thereof, and a functional non-human glutamate transport protein, ~~in~~ or a variant, fragment or functional equivalent thereof[[;]], ~~and wherein said cells are transformed~~ with a recombinant DNA molecule comprising a reporter gene operably linked to a regulatory sequence which responds to a change in intracellular concentration of one or more second messenger substances of a metabotropic glutamate receptor-mediated signal transmission pathway, wherein said response is a change in the expression of a reporter gene in said test mammalian cell, said expression being indicated by production of a reporter gene product;

(b) incubating said transformed test cell population with a candidate agent whose ability to modulate the second messenger activity of the receptor is sought to be determined;

(~~b~~c) measuring the concentration of the reporter gene product in the test cell population; and

(~~c~~d) comparing the concentration of the reporter gene product in said test cell population to the concentration of said reporter gene product in a control cell population, which are identical to the test cells population except that the ~~cells of the~~ control cell population do not express a functional metabotropic glutamate receptor subtype; wherein a higher concentration in said test cell relative to the concentration in said control cell indicates that the test substance has activating activity on said signal transmission pathway, and wherein a lower concentration in said test cell relative to the concentration in said control cell indicates that said test substance has inhibitory activity on said signal transmission pathway.

29. (Currently Amended) The process according to claim 2~~7~~8, wherein said recombinant DNA molecule comprises a regulatory sequence which responds to a change in the concentration of ~~intracellular calcium~~ cyclic AMP brought about by modulation of said receptor.

30. (Canceled)

31. (Currently Amended) A method for identifying candidate therapeutic agents for the treatment of a metabotropic glutamate receptor mediated disorder, comprising:

(a) ~~incubating~~ providing a cell population comprising a plurality of cells co-expressing on a surface thereof at least one metabotropic glutamate receptor subtype glutamate receptor subtype, or a variant, fragment or functional equivalent thereof, and a functional non-human neurotransmitter transport protein, or a variant, fragment or functional equivalent thereof, ~~with a test compound and a known mGluR agonist,~~ wherein said cells population further comprises a reporter construct responsive to a change in one of or more second messenger substances, and wherein said reporter construct comprises a nucleotide sequence encoding a reporter protein operably linked to a responsive regulatory element responsive to a change in a second messenger resulting from activation of said receptor protein[[,]];

(b) incubating said cell population with a test compound and a known mGluR agonist;

(~~b~~c) measuring the expression of the reporter gene ~~product~~ in the presence of the test compound and the agonist and comparing the value to that obtained in the absence of the test compound;

~~(c) selecting a test compound that decreases the expression of the reporter gene product in the presence of the agonist compared to the expression of the reporter gene product in the presence of the test compound alone;~~ and

(d) identifying ~~the selected test compound~~ as a candidate therapeutic agent for treatment of a neurodegenerative disorder, a test compound that decreases the expression of the reporter gene in the presence of the agonist as compared to the expression of the reporter gene in the presence of the test compound alone.

32. (Currently Amended) The method of claim 31, wherein said reporter gene ~~coding sequence~~ is selected from the group consisting of ~~a~~ luciferase, green fluorescent protein, β-lactamase, β-galactosidase, β-glucuronidase; ~~A~~alkaline phosphatase ; blue fluorescent protein, and chloramphenicol acetyl transferase.

33. (Currently Amended) A method for identifying potential allosteric modulators of a mammalian metabotropic glutamate receptor, comprising:

(a) incubating a test cell population comprising a plurality of cells co-expressing on a surface thereof at least one metabotropic glutamate receptor subtype, ~~glutamate receptor subtype~~ or a variant, fragment or functional equivalent thereof, and a functional non-human neurotransmitter transport protein, or a variant, fragment or functional equivalent thereof, with a known amount of a known mGluR

agonist and a test compound, wherein said test cells population further comprises a reporter construct responsive to a change in one of or more second messenger substances, and wherein said reporter construct comprises a nucleotide sequence encoding a reporter protein operably linked to a responsive regulatory element responsive to a change in a second messenger resulting from activation of said receptor protein[[,]];

(b) incubating a control cell population comprising a plurality of cells co-expressing on a surface thereof at least one metabotropic glutamate receptor subtype, and a non-human neurotransmitter transport protein specific for a ligand of said receptor, with a known amount of a known mGluR agonist, wherein said control cells population comprises a reporter construct responsive to a change in one of or more second messenger substances, and wherein said reporter construct comprises a nucleotide sequence encoding a reporter protein operably linked to a responsive regulatory element responsive to a change in a second messenger resulting from activation of said receptor protein,

(c) measuring the expression of the reporter gene ~~product~~ in the presence of the known agonist, i.e. the test cell population, and comparing the value to that obtained in the absence of the known ~~agoinist~~ agonist but in the presence of a test compound alone, i.e. the control cell population;

(d) selecting a test compound that increases or decreases the expression of the reporter gene ~~product~~ in the presence of the test compound alone compared to the expression of the reporter gene product in the presence of the agonist alone; and

(e) identifying the selected test compound as a candidate therapeutic agent for the treatment of a neurodegenerative disease mediated by a metabotropic glutamate receptor subtype and which is susceptible to allosteric modulation by said therapeutic agent.

34. (Original) Host cells transformed with a nucleic acid construct under conditions favoring expression of at least one metabotropic glutamate receptor protein on a surface of said cells and a non-human neurotransmitter transport protein specific for a ligand of said receptor protein.

35. (Currently Amended) A process for determining whether a candidate agent is a metabotropic glutamate receptor antagonist which comprises contacting cells co-expressing a functional metabotropic glutamate receptor and a functional glutamate transporter protein ~~cells~~ with the candidate agent under conditions favoring activation of a functional metabotropic glutamate receptor, ~~with the proviso that said cells co-express a functional glutamate transporter, and detecting any~~ wherein a decrease in metabotropic glutamate receptor activity, ~~as~~ indicat~~inges~~ that the candidate agent is a metabotropic glutamate receptor antagonist.

36. (Currently Amended) A method of screening a plurality of test compounds to identify a candidate compound which inhibits the activation of one or more human metabotropic glutamate receptor subtypes, said method comprising the step of

(a) contacting cells co-expressing at least one metabotropic glutamate receptor subtype and a neurotransmitter transport protein specific for a ligand of said metabotropic glutamate receptor subtype, wherein said cells produce a second messenger response upon activation of the metabotropic glutamate receptor, with ~~the~~ a plurality of test compounds in the presence of a known metabotropic glutamate receptor agonist under conditions suitable for activation of the metabotropic glutamate receptor~~, and~~;

(b) determining whether the extent or amount of activation of the metabotropic glutamate receptor is reduced in the presence of one or more of the test compounds, relative to the extent or amount of activation of the metabotropic glutamate receptor in the absence of said one or more test compounds~~, and if so,~~ ; and

(c) separately determining ~~whether~~ for each ~~such~~ compound ~~inhibits~~ of step (b) the extent or amount of activation of the metabotropic glutamate receptor ~~for each compound in the plurality of compounds~~, so as to identify any such compound ~~in such plurality of compounds which inhibits the activation of the metabotropic glutamate receptor~~ as an inhibitor.

37. (Currently Amended) A process for determining whether a candidate agent is a metabotropic glutamate receptor agonist which comprises contacting a control cell population, comprising cells that do not express a functional metabotropic glutamate receptor protein, and a test cell population, comprising a plurality of cells co-transfected with a nucleic acid encoding a metabotropic glutamate receptor under conditions favoring expression of the metabotropic glutamate receptor on a surface of said transfected cells and a functional glutamate transporter protein, with the candidate agent under conditions favoring activation of the metabotropic glutamate receptor and detecting any increase in human metabotropic glutamate receptor activity relative to a control cell population, wherein such increase ~~as~~ indicatinges that the candidate agent is a metabotropic glutamate receptor agonist.

38. (Currently Amended) A process for determining whether a chemical compound specifically binds to and activates one or more metabotropic glutamate receptor subtypes, which comprises contacting cells producing a second messenger response and co-expressing on their cell surface at least one metabotropic glutamate receptor subtype and a glutamate transporter protein specific for a ligand bound by said metabotropic glutamate receptor subtype, ~~wherein such cells do not normally express the metabotropic glutamate receptor,~~ with the chemical compound under conditions suitable for

activation of the human metabotropic glutamate receptor and measuring the second messenger response in the presence and in the absence of the chemical compound, wherein a change in the second messenger response in the presence of the chemical compound indicat~~inges~~ that the compound activates the metabotropic glutamate receptor subtype~~, with the provisio that said cell also express a glutamate transporter protein specific for a ligand bound by said metabotropic glutamate receptor subtype~~.

39. (Canceled)